

SUBSTITUTE SEQUENCE LISTING

	HADEV	
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Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln

Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly 505 Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn 535 His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 550 <210> 15 <211> 1359 <212> DNA <213> Artificial Sequence <220> <223> Flt1(2-3 deltaB)-Fc(Mut2) <220> <221> CDS <222> (1)..(1359) <400> 15 atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc 48 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser 96 tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc gta gag Cys Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu 20 144 atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga agg gag Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu 35 40 ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt act tta 192 Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu 50 55 240 aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc ata atc Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile 80 65 tgg gac agt aga aag ggc ttc atc ata tca aat gca acg tac aaa gaa 288 Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu 336 ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat ttg tat aag Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys 100 aca aac tat ctc aca cat cga caa acc aat aca atc ata gat gtc caa 384 Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln

Ile	agc Ser 130	aca Thr	cca Pro	cgc Arg	cca Pro	gtc Val 135	aaa Lys	tta Leu	ctt Leu	aga Arg	ggc Gly 140	cat His	act Thr	ctt Leu	gtc Val	432	:
ctc Leu 145	aat Asn	tgt Cys	act Thr	gct Ala	acc Thr 150	act Thṛ	ccc Pro	ttg Leu	aac Asn	acg Thr 155	aga Arg	gtt Val	caa Gln	atg Met	acc Thr 160	480)
tgg Trp	agt Ser	tac Tyr	cct Pro	gat Asp 165	gaa Glu	att Ile	gac Asp	caa Gln	agc Ser 170	aat Asn	tcc Ser	cat His	gcc Ala	aac Asn 175	ata Ile	528	}
ttc Phe	tac Tyr	agt Ser	gtt Val 180	ctt Leu	act Thr	att Ile	gac Asp	aaa Lys 185	atg Met	cag Gln	aac Asn	aaa Lys	gac Asp 190	aaa Lys	gga Gly	576	5
ctt Leu	tat Tyr	act Thr 195	tgt Cys	cgt Arg	gta Val	agg Arg	agt Ser 200	gga Gly	cca Pro	tca Ser	ttc Phe	aaa Lys 205	tct Ser	gtt Val	aac Asn	624	1
acc Thr	tca Ser 210	gtg Val	cat His	ata Ile	tat Tyr	gat Asp 215	aaa Lys	gca Ala	ggc Gly	ccg Pro	ggc Gly 220	gag Glu	ccc Pro	aaa Lys	tct Ser	672	2
tgt Cys 225	gac Asp	aaa Lys	act Thr	cac His	aca Thr 230	tgc Cys	cca Pro	ccg Pro	tgc Cys	cca Pro 235	gca Ala	cct Pro	gaa Glu	ctc Leu	ctg Leu 240	720	Э
Gly	gga Gly	ccg Pro	tca Ser	gtc Val 245	ttc Phe	ctc Leu	ttc Phe	ccc Pro	cca Pro 250	aaa Lys	ccc Pro	aag Lys	gac Asp	acc Thr 255	ctc Leu	768	В
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cac His	gaa Glu	gac Asp 275	Pro	gag Glu	gtc Val	aag Lys	ttc Phe 280	aac Asn	tgg Trp	tac Tyr	gtg Val	gac Asp 285	Gly	gtg Val	gag Glu	86	4
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tac Tyr 305	Arg	gtg Val	gtc Val	agc Ser	gtc Val 310	ctc Leu	acc Thr	gtc Val	ctg Leu	cac His 315	cag Gln	gac Asp	tgg Trp	ctg Leu	aat Asn 320	96	0
ggc Gly	aag Lys	gag Glu	tac Tyr	aag Lys 325	Cys	aag Lys	gtc Val	tcc Ser	aac Asn 330	Lys	gcc Ala	ctc Leu	cca Pro	gcc Ala 335	Pro	100	8
atc Ile	gag Glu	aaa Lys	acc Thr 340	Ile	tcc Ser	aaa Lys	gcc Ala	aaa Lys 345	Gly	cag Gln	ccc Pro	cga Arg	gaa Glu 350	Pro	cag Gln	105	6
gtg Val	Туг	acc Thr 355	Leu	ccc Pro	cca Pro	tcc Ser	cgg Arg 360	Asp	gag Glu	ctg Leu	acc Thr	aag Lys 365	Asn	cag Gln	gtc Val	110	4

ser Leu Thr C	gc ctg gt Cys Leu Va						
gag tgg gag a Glu Trp Glu S 385		y Gln Pro				Thr	
ccc gtg ctg g Pro Val Leu A				Leu Tyr			
gtg gac aag a Val Asp Lys S 4	agc agg tg Ser Arg Tr 120	g cag cag o Gln Glr	ggg aac Gly Asn 425	gtc ttc Val Phe	tca tgo Ser Cys 430	s Ser	gtg 1296 Val
atg cat gag g Met His Glu A 435	gct ctg ca Ala Leu Hi	c aac cad s Asn His 44(Tyr Thr	cag aag Gln Lys	agc cto Ser Let 445	tcc Ser	ctg 1344 Leu
tct ccg ggt a Ser Pro Gly I 450	_						1359
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	2-3 _{deltab})-	FC					
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Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln 115 120

Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val

Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr

Trp Ser Tyr Pro Asp Glu Ile Asp Gln Ser Asn Ser His Ala Asn Ile

Phe Tyr Ser Val Leu Thr Ile Asp Lys Met Gln Asn Lys Asp Lys Gly

Leu Tyr Thr Cys Arg Val Arg Ser Gly Pro Ser Phe Lys Ser Val Asn

Thr Ser Val His Ile Tyr Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser

Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser

His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu

Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr

Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn

Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro

Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln

Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val 360 355 Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val 375 370 Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro 395 390 Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr 410 Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val 420 Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu 435 440 Ser Pro Gly Lys 450 <210> 17 <211> 1389 <212> DNA <213> Artificial Sequence <220> <223> Flt1(2-3)-Fc (Mut3) <220> <221> CDS <222> (1)..(1389) <400> 17 atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc 48 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser 1 96 tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc gta gag Cys Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu 20 144 atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga agg gag Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu 35 40 192 ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt act tta Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu 50 55 60 aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc ata atc 240

Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile

65	70	75	80
		a tca aat gca acg tag e Ser Asn Ala Thr Ty: 90	
		a gtc aat ggg cat ttg Val Asn Gly His Le 11	ı Tyr Lys
		aat aca atc ata ga Asn Thr Ile Ile Asp 125	
		a ctt aga ggc cat ac 1 Leu Arg Gly His Th 140	
		g aac acg aga gtt ca n Asn Thr Arg Val Gl 155	
	Glu Lys Asn Lys	g aga gct tcc gta ago s Arg Ala Ser Val Aro 170	
		c ata ttc tac agt gt n Ile Phe Tyr Ser Va n 19	l Leu Thr
		a gga ctt tat act tg s Gly Leu Tyr Thr Cy 205	
		t aac acc tca gtg ca L Asn Thr Ser Val Hi 220	
		a tct tgt gac aaa ac s Ser Cys Asp Lys Th 235	
	Ala Pro Glu Le	c ctg ggg gga ccg tc 1 Leu Gly Gly Pro Se 250	
		c ctc atg atc tcc cg r Leu Met Ile Ser Ar 5 27	g Thr Pro
		g agc cac gaa gac cc l Ser His Glu Asp Pr 285	
		g gag gtg cat aat gc l Glu Val His Asn Al 300	
		c acg tac cgt gtg gt r Thr Tyr Arg Val Va 315	

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tcc cgg gat gag ctg acc aag aac cag gtc agc ctg acc tgc ctg Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu 370 375 380	gtc 1152 Val
aaa ggc ttc tat ccc agc gac atc gcc gtg gag tgg gag agc aat Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn 385 390 395	ggg 1200 Gly 400
cag ccg gag aac aac tac aag acc acg cct ccc gtg ctg gac tcc Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser 405 410 415	gac 1248 Asp
ggc tcc ttc ttc ctc tac agc aag ctc acc gtg gac aag agc agg Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg 420 425 430	tgg 1296 Trp
cag cag ggg aac gtc ttc tca tgc tcc gtg atg cat gag gct ctg Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu 435 440 445	cac 1344 His
aac cac tac acg cag aag agc ctc tcc ctg tct ccg ggt aaa tga Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 450 455 460	1389
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Cys Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val 20 25 30	Glu
Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg 35 40 45	Glu

Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu

60

Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile 65 70 75 80

55

- Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu 85 90 95
- Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
 100 105 110
- Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Gln
 115 120 125
- Ile Ser Thr Pro Arg Pro Val Lys Leu Leu Arg Gly His Thr Leu Val 130 135 140
- Leu Asn Cys Thr Ala Thr Thr Pro Leu Asn Thr Arg Val Gln Met Thr 145 150 155 160
- Trp Ser Tyr Pro Asp Glu Lys Asn Lys Arg Ala Ser Val Arg Arg Arg 165 170 175
- Ile Asp Gln Ser Asn Ser His Ala Asn Ile Phe Tyr Ser Val Leu Thr 180 185 190
- Ile Asp Lys Met Gln Asn Lys Asp Lys Gly Leu Tyr Thr Cys Arg Val 195 200 205
- Arg Ser Gly Pro Ser Phe Lys Ser Val Asn Thr Ser Val His Ile Tyr 210 215 220
- Asp Lys Ala Gly Pro Gly Glu Pro Lys Ser Cys Asp Lys Thr His Thr 225 230 235 240
- Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe 245 250 255
- Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro 260 265 270
- Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val 275 280 285
- Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr 290 295 300 .

Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val 315 305 310 Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys 330 325 Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser 340 345 Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro 360 355 Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val 375 370 Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly 395 390 385 Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp 410 Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp 420 Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His 440 435 Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 455 <210> 19 <211> 1704 <212> <213> Artificial Sequence <220> <223> Flt1(1-3 $_{R->N}$) (Mut 4) <220> <221> CDS <222> (1)..(1704) <400> 19 48 atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg ctc agc Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser tgt ctg ctt ctc aca gga tct agt tca ggt tca aaa tta aaa gat cct 96 Cys Leu Leu Thr Gly Ser Ser Ser Gly Ser Lys Leu Lys Asp Pro

...

20	25		30
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Gln Cys Arg G		gcc cat aaa tgg Ala His Lys Trp 60	
 		g ctg agc ata act g Leu Ser Ile Thr 75	
		e agt act tta acc s Ser Thr Leu Thr 90	
		e agc tgc aaa tat e Ser Cys Lys Tyr	
		a tct gca atc tat 1 Ser Ala Ile Tyr 125	
Gly Arg Pro E		g atg tac agt gaa n Met Tyr Ser Glu 140	
		g ctc gtc att ccc 1 Leu Val Ile Pro 155	
		a aaa aag ttt cca 1 Lys Lys Phe Pro 170	
		tgg gac agt aga Trp Asp Ser Arg	
	_	a ata ggg ctt ctg n Ile Gly Leu Leu 205	_

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caa acc aat aca atc ata gat gtc caa ata agc aca cca cgc cca gtc

Gln Thr Asn Thr Ile Ile Asp Val Gln Ile Ser Thr Pro Arg Pro Val

aaa tta ctt aga ggc cat act ctt gtc ctc aat tgt act gct acc act Lys Leu Leu Arg Gly His Thr Leu Val Leu Asn Cys Thr Ala Thr Thr

ccc ttg aac acg aga gtt caa atg acc tgg agt tac cct gat gaa aaa Pro Leu Asn Thr Arg Val Gln Met Thr Trp Ser Tyr Pro Asp Glu Lys 265

215

230

245

22

235

270

672

720

768

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					agt Ser											912
					act Thr 310											960
					gtg Val											1008
					aaa Lys											1056
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					tcc Ser											1152
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					gtg Val											1296
					gag Glu											1344
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					acc Thr 470											1440
aac Asn	cag Gln	gtc Val	agc Ser	ctg Leu 485	acc Thr	tgc Cys	ctg Leu	gtc Val	aaa Lys 490	ggc Gly	ttc Phe	tat Tyr	ccc Pro	agc Ser 495	gac Asp	1488
				Trp	gag Glu											1536

acc acg cct ccc gtg ctg Thr Thr Pro Pro Val Leu 515			
aag ctc acc gtg gac aag Lys Leu Thr Val Asp Lys 530			
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Leu His Leu Gln Cys Arg 50	Gly Glu Ala 55	Ala His Lys Trp S 60	er Leu Pro
Glu Met Val Ser Lys Glu 65 70	Ser Glu Arg	Leu Ser Ile Thr L	ys Ser Ala 80
Cys Gly Arg Asn Gly Lys 85	Gln Phe Cys	Ser Thr Leu Thr L	eu Asn Thr 95
Ala Gln Ala Asn His Thr 100	Gly Phe Tyr 105		eu Ala Val 10
Pro Thr Ser Lys Lys Lys 115	Glu Thr Glu 120	Ser Ala Ile Tyr I 125	le Phe Ile
Ser Asp Thr Gly Arg Pro	Phe Val Glu 135	Met Tyr Ser Glu I 140	le Pro Glu

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Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp 385 390 395 400

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr 405 410 415

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp 420 425 430

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu 435 440 445

Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg 450 455 460

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys 465 470 475 480

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp 485 490 495

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys 500 505 510

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser 515 520 525

Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser 530 535 540

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gta gag atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly 35 40 45	206
agg gag ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val . 50 55 60	254
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ctt gtc tta aat tgt aca gca aga act gaa cta aat gtg ggg att gac Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp 145 150 155	542
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acc tgt gca gca tcc agt ggg ctg atg acc aag aag aac agc aca ttt Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe 210 215 220	734
gtc agg gtc cat gaa aag ggc ccg ggc gac aaa act cac aca tgc cca Val Arg Val His Glu Lys Gly Pro Gly Asp Lys Thr His Thr Cys Pro	782

		225					230					235				
					gaa Glu											830
ccc Pro 255	cca Pro	aaa Lys	ccc Pro	aag Lys	gac Asp 260	acc Thr	ctc Leu	atg Met	atc Ile	tcc Ser 265	cgg Arg	acc Thr	cct Pro	gag Glu	gtc Val 270	878
					gac Asp											926
aac Asn	tgg Trp	tac Tyr	gtg Val 290	gac Asp	ggc Gly	gtg Val	gag Glu	gtg Val 295	cat His	aat Asn	gcc Ala	aag Lys	aca Thr 300	aag Lys	ccg Pro	974
cgg Arg	gag Glu	gag Glu 305	cag Gln	tac Tyr	aac Asn	agc Ser	acg Thr 310	tac Tyr	cgt Arg	gtg Val	gtc Val	agc Ser 315	gtc Val	ctc Leu	acc Thr	1022
gtc Val	ctg Leu 320	cac His	cag Gln	gac Asp	tgg Trp	ctg Leu 325	aat Asn	ggc Gly	aag Lys	gag Glu	tac Tyr 330	aag Lys	tgc Cys	aag Lys	gtc Val	1070
					cca Pro 340											1118
					gaa Glu											1166
gat Asp	gag Glu	ctg Leu	acc Thr 370	aag Lys	aac Asn	cag Gln	gtc Val	agc Ser 375	ctg Leu	acc Thr	tgc Cys	ctg Leu	gtc Val 380	aaa Lys	ggc Gly	1214
ttc Phe	tat Tyr	ccc Pro 385	agc Ser	gac Asp	atc Ile	gcc Ala	gtg Val 390	gag Glu	tgg Trp	gag Glu	agc Ser	aat Asn 395	ggg Gly	cag Gln	ccg Pro	1262
					acc Thr											1310
					aag Lys 420											1358
ggg ggg	aac Asn	gtc Val	ttc Phe	tca Ser 435	tgc Cys	tcc Ser	gtg Val	atg Met	cat His 440	gag Glu	gct Ala	ctg Leu	cac His	aac Asn 445	cac His	1406
				Ser	ctc Leu							tga	gcgg	ccg. (C	1453

<210> 22 <211> 458

<212> PRT

<213> Artificial Sequence

<220>

<223> Flt1D2.Flk1D3.FcdeltaC1(a) Receptor

<400> 22

Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser 1 5 10 15

Cys Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu 20 25 30

Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu 35 40 45

Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu 50 55 60

Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile 65 70 75 80

Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu 85 90 95

Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys
100 105 110

Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Val 115 120 125

Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys Leu Val 130 135 140

Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp Phe Asn 145 150 155 160

Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val Asn Arg 165 170 175

Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu Ser Thr 180 185 190

Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys
195 200 205

Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe Val Arg

210 215 220

Val His Glu Lys Gly Pro Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys

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caaccacc atg gtc agc tac tgg gac acc ggg gtc ctg ctg tgc gcg ctg Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu 1 5 10	110
ctc agc tgt ctg ctt ctc aca gga tct agt tcc gga ggt aga cct ttc Leu Ser Cys Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe 15 20 . 25 30	158
gta gag atg tac agt gaa atc ccc gaa att ata cac atg act gaa gga Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly 35 40 45	206
agg gag ctc gtc att ccc tgc cgg gtt acg tca cct aac atc act gtt Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val 50 55 60	254
act tta aaa aag ttt cca ctt gac act ttg atc cct gat gga aaa cgc Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg 65 70 75	302
ata atc tgg gac agt aga aag ggc ttc atc ata tca aat gca acg tac Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr 80 85 90	350
aaa gaa ata ggg ctt ctg acc tgt gaa gca aca gtc aat ggg cat ttg Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu 95 100 105 110	398
tat aag aca aac tat ctc aca cat cga caa acc aat aca atc ata gat Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp 115 120 125	446
atc cag ctg ttg ccc agg aag tcg ctg gag ctg ctg gta ggg gag aag Ile Gln Leu Leu Pro Arg Lys Ser Leu Glu Leu Leu Val Gly Glu Lys 130 135 140	494
ctg gtc ctc aac tgc acc gtg tgg gct gag ttt aac tca ggt gtc acc Leu Val Leu Asn Cys Thr Val Trp Ala Glu Phe Asn Ser Gly Val Thr 145 150 155	542
ttt gac tgg gac tac cca ggg aag cag gca gag cgg ggt aag tgg gtg Phe Asp Trp Asp Tyr Pro Gly Lys Gln Ala Glu Arg Gly Lys Trp Val 160 165 170	590

													agc Ser			638
													gtg Val			686
													gtc Val 220			734
cat His	gaa Glu	aat Asn 225	ggc Gly	ccg Pro	ggc Gly	gac Asp	aaa Lys 230	act Thr	cac His	aca Thr	tgc Cys	cca Pro 235	ccg Pro	tgc Cys	cca Pro	782
gca Ala	cct Pro 240	gaa Glu	ctc Leu	ctg Leu	GJÀ aaa	gga Gly 245	ccg Pro	tca Ser	gtc Val	ttc Phe	ctc Leu 250	ttc Phe	ccc Pro	cca Pro	aaa Lys	830
													aca Thr			878
gtg Val	gtg Val	gac Asp	gtg Val	agc Ser 275	cac His	gaa Glu	gac Asp	cct Pro	gag Glu 280	gtc Val	aag Lys	ttc Phe	aac Asn	tgg Trp 285	tac Tyr	926
gtg Val	gac Asp	ggc Gly	gtg Val 290	gag Glu	gtg Val	cat His	aat Asn	gcc Ala 295	aag Lys	aca Thr	aag Lys	ccg Pro	cgg Arg 300	gag Glu	gag Glu	974
cag Gln	tac Tyr	aac Asn 305	agc Ser	acg Thr	tac Tyr	cgt Arg	gtg Val 310	gtc Val	agc Ser	gtc Val	ctc Leu	acc Thr 315	gtc Val	ctg Leu	cac His	1022
cag Gln	gac Asp 320	tgg Trp	ctg Leu	aat Asn	ggc Gly	aag Lys 325	gag Glu	tac Tyr	aag Lys	tgc Cys	aag Lys 330	gtc Val	tcc Ser	aac Asn	aaa Lys	1070
gcc Ala 335	ctc Leu	cca Pro	gcc Ala	ccc Pro	atc Ile 340	gag Glu	aaa Lys	acc Thr	atc Ile	tcc Ser 345	aaa Lys	gcc Ala	aaa Lys	ggg ggg	cag Gln 350	1118
													gat Asp			1166
													ttc Phe 380			1214
													gag Glu			1262
													ttc Phe			1310
tat	agc	aag	ctc	acc	gtg	gac	aag	agc	agg	tgg	cag	cag	ggg	aac	gtc	1358

Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn Val ttc tca tgc tcc gtg atg cat gag gct ctg cac aac cac tac acg cag Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln aag agc ctc tcc ctg tct ccg ggt aaa tga gcggccgc Lys Ser Leu Ser Leu Ser Pro Gly Lys <210> <211> <212> PRT <213> Artificial Sequence <220> Flt1D2.VEGFR3D3.FcdeltaC1(a)Receptor <223> <400> Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu Cys Ala Leu Leu Ser 5 . Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Gly Arg Pro Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile Ile His Met Thr Glu Gly Arg Glu Leu Val Ile Pro Cys Arg Val Thr Ser Pro Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Ile Gln Leu Leu Pro Arg Lys Ser Leu Glu Leu Leu Val Gly Glu Lys Leu Val Leu Asn Cys Thr Val Trp Ala Glu Phe Asn Ser Gly Val Thr Phe Asp

Trp Asp Tyr Pro Gly Lys Gln Ala Glu Arg Gly Lys Trp Val Pro Glu Arg Arg Ser Gln Gln Thr His Thr Glu Leu Ser Ser Ile Leu Thr Ile His Asn Val Ser Gln His Asp Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn Gly Ile Gln Arg Phe Arg Glu Ser Thr Glu Val Ile Val His Glu 210 · Asn Gly Pro Gly Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys

Thr Thr Pro P	ro Val Leu Asp 405	Ser Asp Gly 410		415	
	al Asp Lys Ser 20	Arg Trp Gln 425		Val Phe Ser 430	
Cys Ser Val M 435	et His Glu Ala	Leu His Asn 440	His Tyr Thr	Gln Lys Ser	
Leu Ser Leu S 450	er Pro Gly Lys 455				
<210> 25 <211> 1377 <212> DNA <213> Artifi	cial Sequence				
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<220> <221> CDS <222> (1)(1377)				
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Cys Leu Leu L	etc aca gga tct eu Thr Gly Ser	agt tcc gga Ser Ser Gly 25	Ser Asp Thr	ggt aga cct Gly Arg Pro 30	96
ttc gta gag a Phe Val Glu M 35	itg tac agt gaa Met Tyr Ser Gli	a atc ccc gaa n Ile Pro Glu 40	att ata cac Ile Ile His 45	atg act gaa Met Thr Glu	144
gga agg gag c Gly Arg Glu L 50	etc gtc att ccc eu Val Ile Pro 55	tgc cgg gtt Cys Arg Val	acg tca cct Thr Ser Pro 60	aac atc act Asn Ile Thr	192
gtt act tta a Val Thr Leu L 65	aaa aag ttt cca ys Lys Phe Pro 70	a ctt gac act o Leu Asp Thr	ttg atc cct Leu Ile Pro 75	gat gga aaa Asp Gly Lys 80	240
cgc ata atc t Arg Ile Ile T	gg gac agt aga rp Asp Ser Arg 85	a aag ggc tto g Lys Gly Phe 90	atc ata tca : Ile Ile Ser	aat gca acg Asn Ala Thr 95	288
Tyr Lys Glu I	ata ggg ctt ctg le Gly Leu Leu .00				336
	aca aac tat cto Thr Asn Tyr Le				384

					ccg Pro												432
					tgt Cys 150												480
					tac Tyr												528
					aaa Lys												576
					ata Ile												624
					tcc Ser												672
ttt Phe 225	gtc Val	agg Arg	gtc Val	cat His	gaa Glu 230	aag Lys	gac Asp	aaa Lys	act Thr	cac His 235	aca Thr	tgc Cys	cca Pro	ccg Pro	tgc Cys 240		720
cca Pro	gca Ala	cct Pro	gaa Glu	ctc Leu 245	ctg Leu	Gly	gga Gly	ccg Pro	tca Ser 250	gtc Val	ttc Phe	ctc Leu	ttc Phe	ccc Pro 255	cca Pro		768
					ctc Leu												816
gtg Val	gtg Val	gtg Val 275	gac Asp	gtg Val	agc Ser	cac His	gaa Glu 280	gac Asp	cct Pro	gag Glu	gtc Val	aag Lys 285	ttc Phe	aac Asn	tgg Trp		864
					gag Glu												912
gag Glu 305	cag Gln	tac Tyr	aac Asn	agc Ser	acg Thr 310	tac Tyr	cgt Arg	gtg Val	gtc Val	agc Ser 315	gtc Val	ctc Leu	acc Thr	gtc Val	ctg Leu 320		960
cac His	cag Gln	gac Asp	tgg Trp	ctg Leu 325	aat Asn	ggc Gly	aag Lys	gag Glu	tac Tyr 330	aag Lys	tgc Cys	aag Lys	gtc Val	tcc Ser 335	aac Asn	;	1008
					ccc Pro											;	1056
cag Gln	ccc Pro	cga Arg 355	gaa Glu	cca Pro	cag Gln	gtg Val	tac Tyr 360	acc Thr	ctg Leu	ccc Pro	cca Pro	tcc Ser 365	cgg Arg	gat Asp	gag Glu	;	1104
ctg	acc	aag	aac	cag	gtc	agc	ctg	acc	tgc	ctg	gtc	aaa	ggc	ttc	tat		1152

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu 370 375	Val Lys Gly Phe Tyr 380
ccc agc gac atc gcc gtg gag tgg gag agc aatPro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn385390	ggg cag ccg gag aac 1200 Gly Gln Pro Glu Asn 400
aac tac aag acc acg cct ccc gtg ctg gac tcc Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser 405 410	gac ggc tcc ttc ttc 1248 Asp Gly Ser Phe Phe 415
ctc tac agc aag ctc acc gtg gac aag agc agg Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg 420 425	tgg cag cag ggg aac 1296 Trp Gln Gln Gly Asn 430
gtc ttc tca tgc tcc gtg atg cat gag gct ctg Val Phe Ser Cys Ser Val Met His Glu Ala Leu 435 440	cac aac cac tac acg 1344 His Asn His Tyr Thr 445
cag aag agc ctc tcc ctg tct ccg ggt aaa tga Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 450 455	1377
<210> 26 <211> 458 <212> PRT <213> Artificial Sequence	
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< 2.2.35 VEGER R.Z F.C. a. 1 t. a. L. ± (a.) Receptor	
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	Cys Ala Leu Leu Ser 15
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<pre><400> 26 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu 1</pre>	Asp Thr Gly Arg Pro
<pre> <400> 26 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu 1 Cys Leu Leu Leu Thr Gly Ser Ser Ser Gly Ser 20 Phe Val Glu Met Tyr Ser Glu Ile Pro Glu Ile </pre>	Asp Thr Gly Arg Pro 30 Ile His Met Thr Glu 45
<pre> <400> 26 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu 1</pre>	Asp Thr Gly Arg Pro 30 Ile His Met Thr Glu 45 Ser Pro Asn Ile Thr 60
<pre> **A00> 26 Met Val Ser Tyr Trp Asp Thr Gly Val Leu Leu 1</pre>	Asp Thr Gly Arg Pro 30 Ile His Met Thr Glu 45 Ser Pro Asn Ile Thr 60 Ile Pro Asp Gly Lys 80

Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr Phe Val Arg Val His Glu Lys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly

Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Arg Asp Glu 355 360 365

Leu Thr Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr 370 375 380

Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn 385 390 395 400

Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe 405 410 415

Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg Trp Gln Gln Gly Asn 420 425 430

Val Phe Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr 435 440 445

Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 450 455

<210> 27

<211> 431

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<213> Artificial Sequence

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Asn Ile Thr Val Thr Leu Lys Lys Phe Pro Leu Asp Thr Leu Ile Pro 35 40 45

Asp Gly Lys Arg Ile Ile Trp Asp Ser Arg Lys Gly Phe Ile Ile Ser 50 60

Asn Ala Thr Tyr Lys Glu Ile Gly Leu Leu Thr Cys Glu Ala Thr Val 65 70 75 80

Asn Gly His Leu Tyr Lys Thr Asn Tyr Leu Thr His Arg Gln Thr Asn 85 90 95

Thr Ile Ile Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser 100 105 110

Val Gly Glu Lys Leu Val Leu Asn Cys Thr Ala Arg Thr Glu Leu Asn 115 120 125

Val Gly Ile Asp Phe Asn Trp Glu Tyr Pro Ser Ser Lys His Gln His 130 Lys Lys Leu Val Asn Arg Asp Leu Lys Thr Gln Ser Gly Ser Glu Met 150 Lys Lys Phe Leu Ser Thr Leu Thr Ile Asp Gly Val Thr Arg Ser Asp Gln Gly Leu Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys 185 Asn Ser Thr Phe Val Arg Val His Glu Lys Gly Pro Gly Asp Lys Thr 200 His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro Ser 215 Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser Arg 235 Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn Ala 265 Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu Tyr 295 Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys Thr 315 Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr Leu 330 Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu Asp Ser 375 370 Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys Ser Arg 395 390 Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu Ala Leu 410 405 His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly Lys 430 425 420